Claims

1. A method for sequencing nucleic acid molecules, comprising the steps of:

a) providing at a first location a plurality of single stranded nucleic acid molecules that have the same sequences as one another and that are hybridised to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;

b) providing at a second location, which is different from the first location, a plurality of single stranded nucleic acid molecules that have the same sequences as one another, but that have different sequences from the sequences of the single stranded nucleic acid molecules at the first location, and that are also hybridised to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;

c) providing each location with a nucleic acid polymerase and a given labelled nucleotide under conditions that allow extension of the primers if a complementary base or if a plurality of such bases is present at the appropriate position in the single stranded nucleic acid molecules;

d) detecting whether or not said labelled nucleotide has been used for primer extension at each location by determining whether or not the label present on said nucleotide has been incorporated into extended primers;

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e) repeating steps c) and d) one or more times so that extended primers comprising a plurality of labels are provided.

2. A method according to claim 1, wherein all or part of the sequence that is obtained in step e) is converted to provide a complementary sequence thereto.

3. A method according to ~~any preceding claim~~ claim 1, wherein if the given nucleotide has been used in primer extension in step d) then this step includes the step of detecting how many of the given nucleotides have been used per extended primer.

4. A method according to ~~any preceding claim~~ claim 1, wherein after step c) excess nucleotides that have not been used in primer extension are removed (e.g. by washing).

5. A method according to ~~any preceding claim~~ claim 1, wherein step d) uses absorption or emission spectrometry.

6. A method according to ~~any preceding claim~~ claim 1, wherein ~~said~~ single stranded nucleic acid molecules, said primers or both of the aforesaid are immobilised.

7. A method according to ~~any preceding claim~~ claim 1 that is used to fully or partially sequence 10 or more nucleic acid molecules having different sequences simultaneously.

8. A method according to ~~any preceding claim~~ claim 1 that is used to fully or partially sequence 100 or more nucleic acid molecules having different sequences simultaneously.

9. A method according to ~~any preceding claim~~ claim 1 that is used to fully or partially sequence 1000 or more nucleic acid molecules having different sequences simultaneously.

10. A method according to ~~any preceding claim~~ claim 1, wherein each of four different nucleotides is used in primer extension.

11. A method according to claim 10, wherein said four different nucleotides are used in a predetermined order in repeated cycles.

12. A method according to claim 10 ~~or claim 11~~, wherein the nucleotides are dATP, dTTP, dGTP and dCTP in labelled form.

13. A method according to claim 10 ~~or claim 11~~, wherein the nucleotides are ATP, UTP, GTP and CTP in labelled form.

14. A method according to ~~any preceding claim~~ claim 1, wherein the detection step is carried out without moving the nucleic acid molecules from the different locations.

15. A method as described in ~~any preceding claim~~ claim 1 with the exception that double stranded nucleic acid molecules having nicks therein are provided at the

first and/or second locations instead of providing single stranded molecules hybridised to primers.

16. A method as described in ~~any preceding claim~~ claim 1 with the exception that only one nucleic acid molecule is provided at the first and/or second locations.

17. A method for sequencing nucleic acid molecules, comprising the steps of:

a) providing at a first location a plurality of single stranded nucleic acid molecules that have the same sequences as one another and that are hybridised to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;

b) providing at a second location, which is different from the first location, a plurality of single stranded nucleic acid molecules that have the same sequences as one another, but that have different sequences from the sequences of the single stranded nucleic acid molecules at the first location, and that are also hybridised to primers in a manner to allow primer extension in the presence of nucleotides and a nucleic acid polymerase;

c) providing each location with a nucleic acid polymerase and a given nucleotide in labelled and unlabelled form under conditions that allow extension of the primers if a complementary base or if a plurality of such bases is present at the appropriate position in the single stranded nucleic acid molecules;

d) detecting whether or not said labelled nucleotide has been used for primer extension at each location by determining whether or not the label present on said nucleotide has been incorporated into extended primers;

e) repeating steps c) and d) one or more times.

18. An apparatus for performing a method according to any preceding claim, the apparatus comprising a plurality of nucleotides, a nucleic acid polymerase and detection means for performing step d) of claim 1 or an equivalent step for any of claims 15 to 17, the detection means being adapted to distinguish between said different locations.

19. An apparatus according to claim 18 comprising means for removing excess nucleotides from the first and second locations (e.g. washing means).

20. An apparatus according to claim 19 or claim 18 that is automated to allow repeated cycles of primer extension and detection.

21. A method of sequencing a target nucleic acid comprising:

(a) hybridizing the target nucleic acid to a primer whereby the target nucleic acid can serve as a template for extension of the 3' end of the primer;

(b) incubating the hybridized target nucleic acid/primer with a polymerase and a type of nucleotide bearing a label under conditions supporting template-directed extension of the primer if the nucleotide type can be incorporated as the complement of a corresponding nucleotide of the target;

(c) measuring first label incorporated into the primer to determine whether, and if so, by how many base increments, the primer has been extended by incorporated of the nucleotide type;

(d) incubating the hybridized primer/target nucleic acid with a different type of nucleotide bearing a label under conditions supporting template-directed extension of the primer if the different nucleotide type can be incorporated so as to be complementary to a corresponding nucleotide in the target;

(e) measuring incremental label incorporated into the primer due to the previous incubating step to determine whether, and if so, by how many base increments, the primer has been extended by incorporation of the different nucleotide type; and

(f) repeating steps (b) – (e) until a desired portion of the target sequence can be determined from the incremental base additions to the primer.

22. A method according to claim 21 which is a method according to any of claims 1 to 14, 16 or 17.

23. A method according to claim 21 ~~or claim 22~~ with the exception that instead of hybridizing a target nucleic acid molecule to a primer and extending the primer with labelled nucleotides, a nick is introduced into a double-stranded nucleic acid molecule and the nick is extended using nick translation and labelled nucleotides.

24. The invention substantially as hereinbefore described.